THE ABSENCE OF HYPERPLASIA OF THE REMAINDER OF THE THYROID IN DOGS AFTER PIECEMEAL REMOVAL OF THIS GLAND. AUTO-TRANSPLANTATION OF THE THYROID IN PARTIALLY THYREOIDECTOMIZED ANIMALS.

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I WOULD here express my thanks to Dr. Halsted,[1] at whose suggestion these experiments were conducted.

Dr. Halsted in 1887 and 1888 showed that in dogs hypertrophy took place in the remaining gland after small pieces of a lobe had been removed.

In the experiments which follow, the manner in which the wounds healed did not seem to affect in any way the behavior of the remainder of the thyroid in the necks of the dogs.

The operation of piecemeal removal was performed on 39 dogs, and the wounds, with few exceptions, healed absolutely *per primam.* Only in one of these 39 dogs did the remainder of the thyroid present a picture of marked glandular hyperplasia.

In 20 dogs the wounds were left open to heal with suppuration. Neither hyperplasia nor hypertrophy were observed in the remaining thyroids of these dogs. Hypertrophy is used to denote measureable increase in the size of the remaining thyroid; hyperplasia signifies changes in the histological picture.

THE EEFECT UPON THE REMAINING GLAND IN THE 39 DOGS OF THE ASEPTIC SERIES, TABLE 1. Dogs 1 to 11; 101 to 124; 501; 701 to 703. In this series the pieces removed at the first operation varied in size. The largest amount removed at the first operation was one and three-quarter lobes; the smallest was approximately one-fifth of one lobe.

In dogs Nos. 120, 121, 123, 124, and 501 no transplantations were made at the first operation; in the remaining 34 dogs autotransplantation was the invariable rule at the first operation.

Of 36 dogs only 3 of the pieces obtained at the second operation or at autopsy differed microscopically from the pieces removed at the first operation. In these three dogs the change was from early glandular hyperplasia to normal.

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[1] Dr. Halsted in a paper on Reconsideration of the Question of Experimental Hypertrophy of the Thyroid Gland, and the Effect of Excision of this Organ upon Other of the Ductless Glands, delivered before the Congress of Physicians and Surgeons, Washington, May, 1913, alluded to the experiments which are herewith reported. See Amer. Jour. Med. Sci., 1914, No. 1, vol. clxvii, p. 58 and 59.

Dog No. 1. The inferior fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 81 days later at the second operation was normal.

Dog No. 9. The inferior one-fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 66 days later at the second operaation was normal.

Dog No. 102. The inferior one-fourth of the left lobe and the inferior two-fifths of the right lobe removed at the first operation showed early glandular hyperplasia. The pieces obtained when the animal was sacrificed 94 days after the first operation were found to be normal.

There was no change in the structure of the remaining gland in 33 dogs during the intervals between the first and second operation or autopsy. The intervals between the first and second removals were: 41, 41, 62, 64, 30, 42, 84, 66, 96, 114, 21, 21, 61, 50, 22, 30, 15, 16, 21, 83, 84, 75, 23, 59, 57, 30, 23, 20, 20, 34, 87, 33, and 62 days.

The specimens removed from the following three dogs at the first operation were lost.

Dog No. 109. The pieces obtained at autopsy 24 days after the first operation were normal in structure. Amount of privation at the first operation was one lobe.

Dog No. 118. One and one-third lobes removed at first operation. Piece removed 58 days after first operation was normal.

Dog No. 122. Two-thirds of one lobe removed at first operation. Piece removed 153 days after first operation was normal.

The remaining glands in 18 dogs did not undergo a change in size or structure during the intervals between the second and third operations, or during the intervals between the second operations and autopsies. The intervals between the second and third operations or autopsies were: 71, 105, 129, 95, 80, 85, 63, 94, 84, 51, 42, 54, 55, 24, 54, 25, 12, and 25 days.

In one dog the remaining gland removed at the third operation showed a structural change:

Dog No. 114. The inferior fifth of the right lobe removed at the first operation was normal. At operation II, 84 days after first operation, the entire left lobe and one-half of the remaining four-fifths of the right lobe were removed. Total privation, one and three-fifths lobes. The pieces removed at the second operation were normal. The remaining two-fifths of the right lobe removed when the animal was sacrificed 53 days after the second operation, 137 days after the first operation, had not increased in size, but on examination presented a picture of marked glandular hyperplasia.

The small piece of one lobe remaining to each of 8 dogs at the fourth operation had, with two exceptions, undergone no change in size or structure.

In six dogs (Nos. 1, 2, 3, 4, 5, and 7) the pieces obtained at the fourth operation presented the same histological picture as those from the third operation. The intervals between the third and fourth operations were: 98, 104, 79, 91, 101 and 58 days. The total number of days between the first and fourth operations on these dogs were: 250, 251, 249, 248, 245, and 185 days.

Dog No. 1. Operation I. Deprived of one-fourth of left lobe. Diagnosis: early glandular hyperplasia. Operation II, eighty-one days after the first, deprived of remaining three-fourths of left lobe. Diagnosis: normal. Operation III, seventy-one days after second, and 152 days after first operation, deprived of two-thirds of the right lobe. Diagnosis: normal. Total privation now one and two-thirds lobes. Operation IV, 98 days after third and 250 days after the first operation. Remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 2. Operation I. Inferior one-third of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, remaining two-thirds of left lobe and the inferior one-fifth of right lobe removed. Diagnosis: normal. Total privation, one and one-fifth lobes. Operation III, 105 days after the second and 146 days after the first operation, two-thirds of the remaining four-fifths of the right lobe removed. Total privation, one and eleven-fifteenth lobes. Diagnosis: normal. Operation IV, 104 days after the third and 250 days after the first operation, the remaining four-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 3. Operation I. Inferior one-half of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, the remaining one-half of left lobe and the inferior one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 129 days after the second and 170 days after the first operation. One-third of the remaining one-half of right lobe removed. Amount of privation, one and two-thirds lobes. Diagnosis: normal. Operation IV, 79 days after the third and 249 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 4. Operation I. Entire left lobe removed. Diagnosis: normal. Operation II, 62 days after the first. Inferior one-fifth of right lobe removed. Diagnosis: normal. Amount of privation, one and one-fifth lobes. Operation III, 95 days after the second and 157 days after the first operation. One-third of the remaining four-fifth of the right lobe removed. Diagnosis: normal. Amount or privation, one and seven-fifteenths lobes. Operation IV, 91 days after the third and 248 days after the first operation. Remaining eight-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 5. Operation I. Inferior half of left lobe removed. Diagnosis: normal. Operation II, 64 days after the first. The remaining one-half of left and one-half of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes.

Operation III, 80 days after the second, 144 days after the first operation. One-third of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and two-thirds lobes. Operation IV, 101 days after the third and 245 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 7. Operation I. Entire left lobe removed. Diagnosis: early glandular hyperplasia. Operation II, 42 days after the first. Inferior one-fourth of right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and one-fourth lobes. Operation III, 85 days after the second and 127 days after the first operation; one-half of the remaining three-fourths of the right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and five-eighths lobes. Operation IV, 58 days after the third and 185 days after the first operation. Remaining three-eighth of right lobe removed. Diagnosis: early glandular hyperplasia.

The remaining gland in two dogs (Nos. 9 and 11) showed a structural change at the fourth operations; a change from normal to early glandular hyperplasia.

Dog No. 9. Operation I. Inferior one-fourth of left lobe removed. Diagnosis: normal. Operation II, 66 days after the first operation. Remaining three-fourths of left lobe and one-third of right lobe were removed. Diagnosis: normal. Amount of privation, one and one-third lobes. Operation III, 94 days after the second and 160 days after the first operation. Two-thirds of the remaining two-thirds of right lobe removed. Diagnosis: normal. Amount of privation, one and seven-ninths lobes. Operation IV, 76 days after the third operation and 236 days after the first. Remaining two-ninth of right lobe removed. Diagnosis: very early glandular hyperplasia.

Dog No. 11. Operation I. Inferior one-third of left and inferior one-third of right lobe removed. Diagnosis: normal. Operation II, 96 days after the first operation. The remaining two-thirds of the right lobe and one-fourth of the remaining two-thirds of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 51 days after the second and 147 days after the first operation; one-fifth of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and three-fifths lobes. Operation IV, 39 days after the third and 186 days after the first operation. The remaining two-fifths of right lobe removed. Diagnosis: very early glandular hyperplasia.

Behavior of the Remaining Gland in Dogs Whose Neck Wounds were Left Open and Healed with Suppuration. Table II. Dogs 301 to 320. The operation of piecemeal removal was performed by cutting through hair and skin, observing no aseptic precautions and leaving the wound open. All of the cervical wounds in the dogs of this series healed with suppuration.

In this series of 20 dogs, the pieces removed at the first operations were diagnosed as follows: normal, 9; very early glandular hyperplasia, 2; early glandular hyperplasia, 7; marked glandular hyperplasia, 2.

The sizes of the pieces removed at the first operation varied from one-fifth of one lobe to one and five-twelfths lobes. The longest interval between the first and second removals was 58 days; the shortest interval 10 days. The diagnoses of the respective pieces removed at the second operation were the same as the diagnoses of the pieces removed at the first operation on the same dogs, except in two cases.

Dog No. 311. Operation I. Left lobe removed. Diagnosis: early glandular hyperplasia. At autopsy 31 days later the remaining right lobe was found to be normal in structure.

Dog No. 314. Diagnosis of left lobe removed at first operation: early glandular hyperplasia. Diagnosis of the remaining right lobe removed 50 days after first operation: normal.

No change in size or structure was observed in the pieces of the remaining glands from 18 dogs removed at the second operation. The intervals between the first and second operations were: 40, 10, 41, 14, 29, 37, 18, 22, 49, 42, 11, 50, 45, 26, 52, 52, 58, and 52 days.

In dog No. 301, a piece of the remaining left lobe removed at the third operation, 90 days after the first, showed no change in structure or size.

In Dog No. 303 (58 days' interval between the first operation and sacrifice of the dog), the remaining one-half of right lobe showed no change in structure or size.

In Dog No. 306 (76 days' interval between the first operation and sacrifice of the animal), the remaining right lobe showed no change in size or structure.

Dog No. 319 gave birth to five puppies 54 days after one and five-twelfths lobes had been removed. The remaining seven-twelfths of the right lobe, obtained when the animal was sacrificed 4 days after delivery, showed no change in size or structure. Diagnosis of pieces first removed: normal. Diagnosis of pieces obtained when the dog was sacrificed 58 days after the first operation normal.

AUTOTRANSPLANTATION OF THE THYROID GLAND.

Of forty-two transplantations, nineteen were successful. The amount of privation of thyroid gland in the animals yielding the living graft varied from one-fifth of one lobe to one and seven-ninths lobes.

Two-thirds of one lobe were removed from dog No. 11, and a portion of this piece was transplanted at the same operation. The graft was not removed at the second operation nor at the third, when the gland in the neck was reduced in amount to four-fifteenths of one lobe. The graft was obtained at the fourth operation when it had been in the abdominal cavity wall for six months; it had changed from normal to very early glandular hyperplasia. The four-fifteenths of the one remaining lobe in the neck of this dog had undergone the same change.

The oldest graft was obtained from dog No. 9, approximately seven and one-half months after implantation and had changed from normal to very early glandular hyperplasia. The thyroid in the neck had been reduced from one and three-fourths lobes to two-ninths of one lobe.

Two implantations were made into dog No. 122 at the first operation when two-thirds of one lobe had been removed. These grafts were recovered five months and twenty-five days after implantation, when there remained to the dog only two-thirds of one thyroid lobe.

The transplantation of round cylinder-shaped pieces of gland, obtained by using a sharp punch, gave the most convincing results. These pieces of gland were uniform in size and measured 5 x 4 mm.

Grafts at body temperature placed into freshly made pockets which contained no blood yielded the best results. After cutting through the anterior sheath of the rectus abdominis muscle, the median border of the muscle was pushed aside and a pocket made by opening and closing the jaws of a fine-pointed artery clamp. Great care was taken to maintain a bloodless dissection.

THE EFFECT OF AUTOTRANSPLANTATIONS UPON THE CERVICAL THYROIDS.

No transplantations were made in the 20 dogs of the series in which no antiseptic precautions were observed. Table II, dogs 301 to 320. Not in one of these dogs did the remaining gland undergo a structural change after pieces of various sizes had been removed.

No transplantations were made in 5 dogs of the aseptic series: Nos. 120, 121, 123, 124, and 501. The intervals between the first operations and autopsies were 30, 23, 20, 20, and 34 days. The control specimens removed at the first operations in these dogs were the same structurally as the pieces obtained when the animals were sacrificed.

In 23 dogs the grafted tissue was absorbed.

The greater part of the one-fourth of the left lobe removed from dog No. 1 at the first operation was transplanted. This graft had been completely absorbed when searched for at the second operation 81 days after the first. A greater part of the remaining three-fourths of the left lobe was transplanted at the second operation. This graft when searched for 169 days after implantation could not be found.

Dog No. 2. A greater part of the remaining two-thirds of the right lobe removed at the second operation was transplanted. The graft when searched for at the fourth operation 209 days after the second had been absorbed.

Dog No. 3. Graft transplanted at first operation and searched for at the second operation 41 days after the first had been absorbed. Operation II. No transplantation. Operation III. A small piece of the piece removed from the remaining one-half of the right lobe was transplanted. This graft, 79 days later, had been etirely replaced by connective tissue.

Dog No. 4. The three transplants were absorbed. They were searched for 62, 95, and 91 days after implantation.

Dog No. 5. Greater part of the one-half of the left lobe removed at the first operation was transplanted. Operation II, 64 days after the first. No trace of graft. Greater part of one-half of right lobe transplanted. Operation III, 80 days after the second. Graft replaced by connective tissue.

The control specimens of thyroids removed from 10 dogs at the first operations were hyperplastic (dogs Nos. 1, 7, 9, 10, 101, 102, 105, 110, 113, and 701). Transplantation was the rule at the first operations on these dogs with hyperplasic glands. In 3 of the 10 dogs the remaining thyroid in the neck of the animals changed from the hyperplastic type to normal. The grafts in 2 of the 3 dogs were absorbed, while in the third a living graft was obtained when the dog was sacrificed (Dog No. 9). In 7 of the 10 dogs the grafts were absorbed, except in one case, dog No. 113. The graft in this dog was in a perfect state of preservation when removed 137 days after implantation. There was no change in the grade of hyperplasia in the remaining cervical thyroids of the 7 dogs in question, hyperplastic at the first and last removals.

Two experiments (dogs Nos. 9 and 11) tend to show that the grafted thyroid undergoes a change in structure similar to the change in the remaining thyroid in the neck of the dog.

Dog No. 9. Two grafts in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations. The remaining two-ninths of the right lobe underwent the same change.

Dog No. 11. The remaining two-fifths of the right lobe and the graft in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations.

THE ACCESSORY THYROIDS IN DOGS PARTIALLY DEPRIVED OF THE THYROID GLAND.

Accessory thyroid glands were searched for and found in dogs 9, 11, 101, 113, 114, 118, 306, 318, 230, and 701. The accessory thyroids always presented precisely the same histological picture as the remains of the thyroid gland in the neck.

SUMMARY.

1. One and three-fourths of the dog's thyroid gland may be removed without appreciably affecting the remainder of the gland.
2. In only 3 of the 59 dogs on which the operation of piecemeal removal was performed did the remaining gland change from a normal to a hyperplastic state. Dogs Nos. 9, 11, and 114.
3. In 5 of the 59 dogs the remaining gland reverted from the early hyperplastic state to the normal state. Dogs Nos. 1, 9, 102, 311, and 314.
4. Where a diagnosis of some degree of hyperplasia was made at the first operation, the pieces removed from the same dogs at subsequent operations had not undergone further hyperplasia.
5. Of the pieces removed from 56 dogs at the first operation, 58 per cent. were normal, 32 per cent. showed early glandular hyperplasia, 5 per cent. marked glandular hyperplasia, and 5 per cent. very early glandular hyperplasia.
6. Definite increase in the size of the remaining gland (hypertrophy) was not observed.
7. The remains of the thyroid lobes, the accessory thyroids, and the successful grafts in a given dog, presented the same histological picture.
8. In no dog was myxedema or tetany observed in which as much as one-fourth of the thyroid and one parathyroid gland were preserved.

PITUITARY DISEASE: A CLINICAL STUDY OF THREE CASES.

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The main purpose of this paper is to record and comment upon several cases of pituitary disorder which present noteworthy clinical features. The literature of this complex subject has become so extensive that an attempt to epitomize it cannot be made here.